PREFRONTAL METABOLIC ABNORMALITIES IN MAJOR DEPRESSIVE DISORDER: A PROTON MAGNETIC RESONANCE SPECTROSCOPY STUDY.


Introduction

Advanced magnetic resonance imaging techniques, such as proton magnetic resonance spectroscopy (H-MRS), have helped to further understanding the physiopathology of MDD and to shed light on mechanisms underlying depressive disorder. Several studies have applied H-MRS to study metabolites levels in acute depression. Overall, the evidence suggests contrasting findings depending on the location of VOI: decreased levels of Glx (a composite measure of glutamate and glutamine) in anterior brain regions such as ACC and VMPFC. This pattern seems to revert in recovered depressed patients by displaying increased levels or by normalizing Glx. NAA and Cho increases have been associated with clinical improvement. However, the possibility that persistent metabolic abnormalities cannot be excluded, yielding to the necessity to study these measures at different phases of the illness.

Purpose of the study

To investigate the effects entailed by the course of MDD on the concentrations of glutamatergic metabolites, N-Acetil-Aspartate (NAA), Inositol and Choline-containing compounds (GPC and GPC+PCh) in a single voxel proton magnetic resonance spectroscopy (1H-MRS) centred on the ventromedial prefrontal cortex (VMPFC). We hypothesize that metabolic changes will occur in this area because of the progression of the illness.

Methods

Participants

10 patients presenting a first depressive episode were compared to those with multiple past episodes—split into euthymic recurrent (n=13) and chronically depressed patients (n=19). All patients were on medication (TAU).

Demographic, clinical and concomitant treatment data were collected, including age, gender, personal and familiar history of psychiatric disorders. Likewise, other clinical data relevant to the study were recorded, such as number of previous episodes, age at first depressive episode, melancholic features, and medical history.

Depression severity was assessed with HDRS.

Data Acquisition

Participants underwent scanning using a 3T proton MRS. Spectra were acquired from a ventromedial prefrontal single voxel (including a portion of the anterior cingulate cortex).

Analyses

1H-MRS data were post-processed and analysed with the LCMModel software.

Statistical analyses were performed in SPSS version 17. Group demographics and clinical characteristics were compared by one-way ANOVA. The available MRS measures were analysed with multivariate analysis using Wilk’s Lambda, and posthoc comparisons (Bonferroni test).

Results

Table 1. Demographics and clinical characteristics of participants.

<table>
<thead>
<tr>
<th></th>
<th>First MD Episode</th>
<th>Recurrent MDD</th>
<th>Chronic MDD</th>
</tr>
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<tbody>
<tr>
<td>Age</td>
<td>43.8</td>
<td>41.1</td>
<td>50.1</td>
</tr>
<tr>
<td>% Females*</td>
<td>50</td>
<td>94</td>
<td>79</td>
</tr>
<tr>
<td>HDRS</td>
<td>13</td>
<td>4.2</td>
<td>2.1</td>
</tr>
<tr>
<td>Age at onset*</td>
<td>43.8</td>
<td>25.1</td>
<td>28.9</td>
</tr>
<tr>
<td>Num. of previous episodes</td>
<td>NA</td>
<td>6.1</td>
<td>7.1</td>
</tr>
<tr>
<td>Time since illness onset (yrs)</td>
<td>NA</td>
<td>19.9</td>
<td>23.1</td>
</tr>
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</table>

Figure 2. Representative images of an individual 1H-MRS spectrum after analysis by LCMModel

Figure 3. Absolute quantification of various ventromedial prefrontal metabolites

Summary

✓ This is the first study approaching regional cerebral metabolite concentrations in PF brain tissue among different phases of MDD, and provide evidence of neuronal changes in the VMPFC over the course of the illness.

✓ Higher values of Glutamate/Glutamine at the beginning of the disorder and their progressive decrement replicate and extend previous MRS studies in MDD, demonstrating reductions in Glutamate levels in the ACC and PFC.

✓ NAA concentration showed a continuous decrement related with disease stage, which may account for histopathological changes that occur as the disorder progresses.

An opposite pattern was observed for Choline concentrations: first-episode patients showed the lowest levels of Choline containing compounds and chronic patients the highest. A previous study has also recently reported Choline containing compounds (GPC & GPC + PCh) being significantly increased in patients with a high past illness burden.

References

1 Hasler et al. 2007, Arch Gen Psychiatry 64(2):193-200.
3 Hasler et al. 2005, Biol Psychiatry 58:969-975.

No conflicts of interest to declare.